PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference NC10009/WO	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/GB2004/050046	International filing date *(day/month/year)* 23.12.2004	Priority date *(day/month/year)* 24.12.2003
International Patent Classification (IPC) or national classification and IPC INV. C07D413/04 C07D413/06 C07D413/12 A61K31/4245		
Applicant PROSIDION LIMITED et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 5 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in celectronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☒	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand 24.10.2005	Date of completion of this report 03.04.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Samsam Bakhtiary, M Telephone No. +49 89 2399-8556

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/050046

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1(b))
   ☐ publication of the international application (under Rule 12.4)
   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-63 as originally filed

   Claims, Numbers

   1-16 received on 28.10.2005 with letter of 24.10.2005

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. II Priority

1. ☒ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

   ☒ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 12-16

   because:

   ☒ the said international application, or the said claims Nos. 12-16 only with regard of industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

   ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

   ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

   ☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/050046

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-16
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-16
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-11
	No:	Claims	12-16

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 12-16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

2. The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search has been restricted to:

The compounds given in Formula I of claim 1, where:
- V is the formula of claim 2, W = N; X and Y are N or O
- A is $(CH2)_n$, n=0

The amendments made namely introducing features of claims 2,3, 4,7 and 8 into claim 1 and introducing the preferred embodiments where A is $(CH2)_n$, n=0 (see description page 3, line 43 and page 5, line 43), leads that this limited scope has been searched.
Claim 10 seems to correspond to original claim 17.
No added subject matter seems to occur.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

D1: WO 98/17652 A (BOEHRINGER INGELHEIM PHARMA KG; BOEHRINGER INGELHEIM INTERNATIONAL GMB) 30 April 1998 (1998-04-30)

D2: WO 01/12627 A (NPS PHARMACEUTICALS, INC; VAN WAGENEN, BRADFORD, C; STORMANN, THOMAS,) 22 February 2001 (2001-02-22)

D3: WO 02/068417 A (NPS PHARMACEUTICALS, INC; SLASSI, ABDELMALIK; VAN WAGENEN, BRADFORD; S) 6 September 2002 (2002-09-06)

D4: US-B1-6 239 160 (TIEBES JOERG ET AL) 29 May 2001 (2001-05-29)

D5: WILLIAMS J P ET AL: "A solution-phase combinatorial synthesis of selective dopamine D4 ligands" COMBINATORIAL CHEMISTRY AND HIGH THROUGHPUT SCREENING, HILVERSUM, NL, vol. 3, no. 1, February 2000 (2000-02), pages 43-50, XP002280990 ISSN: 1386-2073

D6: WO 00/24735 A (DOW AGROSCIENCES LLC) 4 May 2000 (2000-05-04)

D7: WO 00/35913 A (AVENTIS CROPSCIENCE GMBH) 22 June 2000 (2000-06-22)

D8: WO 97/46556 A (MERCK & CO., INC; BIFTU, TESFAYE; FENG, DANQING, DENNIS; FISHER, MICHA) 11 December 1997 (1997-12-11)

D9: WO 2004/060362 A (MILLENNIUM PHARMACEUTICALS, INC; SCARBOROUGH, ROBERT, M; PANDEY, ANJAL) 22 July 2004 (2004-07-22)

2. Novelty

The claimed subject matter of this application is concerned with derivatives useful against satiety or obesity or diabetes.

The documents D3-D7 (see search report for appropriate location of in document) disclose specific compounds that do not affect novelty of the claimed subject matter.
We agree with the analysis made by the Applicant, indeed by limiting n=2 or 3 in claim 1, novelty is restored.

These compounds do not have the same activity as those of this application, therefore are only relevant against novelty.

3. Inventive step

Documents D1 and D2 disclose compounds having different pharmaceutical activities, namely the usefulness against neurodegenerative disorders such as diabetic neuropathic disorders (D1, page 66,line 17-page 67, line 1; D2, page 5, lines 19-22).
The closest prior art may be considered as being D8, which disclose compounds useful for the treatment of diabetes and/or obesity.

The problem to be solved by this application would be to provide novel derivatives useful against diabetes and/or obesity.

In view of the drastic stuctural differences from the compounds of D8 and those claimed in this application, the skilled man would not obviously derive to the claimed subject matter.

Re Item VI
Certain documents cited

Document D9, cited a PX in the search report may become relevant if this application is further proceeded in european phase.

Re Item VII
Certain defects in the international application

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D7,D9 is not mentioned in the description, nor are these documents identified therein.

Re Item VIII

Certain observations on the international application

For the assessment of the present claims 12-16 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

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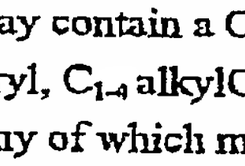
WHAT IS CLAIMED IS:

1. A compound of formula (I), or a pharmaceutically acceptable salt thereof:

$$R^1\text{-}V\text{-}B\text{-}R^2$$

(I)

wherein V represents a 5-membered heteroaryl ring of the formula:



wherein W is N and one of X and Y is N and the other is O;

B is -CH=CH- or $(CH_2)_n$, where one of the CH_2 groups may be replaced by O, NR^5, $S(O)_m$, C(O) or $C(O)NR^{12}$;

n is 2 or 3;

m is independently 0, 1 or 2;

R^1 is 4-pyridyl optionally substituted by 1 or 2 halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-7} cycloalkyl, aryl, OR^6, CN, NO_2, $S(O)_mR^6$, $CON(R^6)_2$, $N(R^6)_2$, $NR^{10}COR^6$, $NR^{10}SO_2R^6$, $SO_2N(R^6)_2$, 4- to 7-membered heterocyclyl or 5- or 6-membered heteroaryl groups;

R^2 is 4- to 7-membered cycloalkyl substituted by R^3, $C(O)OR^3$, $C(O)R^3$ or $S(O)_2R^3$, or 4- to 7-membered heterocyclyl, containing one or two nitrogen atoms which is unsubstituted or substituted by $C(O)OR^4$, $C(O)R^3$, $S(O)_2R^3$, $C(O)NHR^4$, $P(O)(OR^{11})_2$ or a 5- or 6-membered nitrogen containing heteroaryl group;

R^3 is C_{3-8} alkyl, C_{3-8} alkenyl or C_{3-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be optionally substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^4 is C_{2-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^5 is hydrogen, $C(O)R^7$, $S(O)_2R^8$, C_{3-7} cycloalkyl or C_{1-6} alkyl optionally substituted by OR^6, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-2} alkyl, C_{1-2} fluoroalkyl, OR^6, CN, $N(R^6)_2$ and NO_2;

R^6 are independently hydrogen C_{1-4} alkyl, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^9, CN, SO_2CH_3, $N(R^{10})_2$ and NO_2; or a group $N(R^{10})_2$ may form a 4- to 7-membered heterocyclic ring optionally containing a further heteroatom selected from O and NR^{10};

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R^7 is hydrogen, C_{1-4} alkyl, OR^6, $N(R^6)_2$, aryl or heteroaryl;
R^8 is C_{1-4} alkyl, C_{1-4} fluoroalkyl, aryl or heteroaryl;
R^9 is hydrogen, C_{1-2} alkyl or C_{1-2} fluoroalkyl;
R^{10} is hydrogen or C_{1-4} alkyl;
R^{11} is phenyl; and
R^{12} is hydrogen, C_{1-4} alkyl or C_{3-7} cycloalkyl;
provided that the compound is not:

a) 4-(5-piperidin-4-yl-[1,2,4]oxadiazol-3-yl)pyridine;
b) 4-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-yl)piperidine-1-carboxylic acid 'butyl ester; or
c) 4-[5-(4-butylcyclohexyl)-[1,2,4]oxadiazol-3-yl]pyridine.

2. A compound according to claim 1, or a pharmaceutically acceptable salt thereof; wherein R^1 is 4-pyridyl optionally substituted by halo, C_{1-4} alkyl, C_{1-4} alkoxy or CN.

3. A compound according to claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein R^2 is a 4- to 7-membered cycloalkyl substituted by R^3, or 4- to 7-membered heterocyclyl containing one nitrogen atom which is substituted by $C(O)OR^4$.

4. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_{3-8} alkyl which may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl.

5. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^4 is C_{2-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, 5- to 6-membered heteroaryl containing one or two nitrogen atoms, C_{1-4} alkylC_{3-7} cycloalkyl or C_{1-4} alkylaryl, any of which may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6 and CO_2C_{1-4} alkyl.

6. A compound according to claim 5, or a pharmaceutically acceptable salt thereof, wherein R^4 is C_{3-6}alkyl optionally substituted with up to 5 fluoro or chloro atoms, and which may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl.

7. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^5 is C_{1-4} alkyl.

8. A compound as defined in any one of Examples 1, 3 to 5, 10 to 13, 16 to 39, 41, 42, or 52 to 132, 134,135, or 147 to 149 or a pharmaceutically acceptable salt thereof.

9. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:

B is -CH=CH- or $(CH_2)_m$, where one of the CH_2 groups may be replaced by O, NR^5, $S(O)_m$ or C(O);

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n is 2 or 3;

m is independently 0, 1 or 2;

R^2 is 4- to 7-membered heterocyclyl containing one nitrogen atom which is substituted by $C(O)OR^4$ or a 6-membered nitrogen containing heteroaryl group;

R^4 is C_{2-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

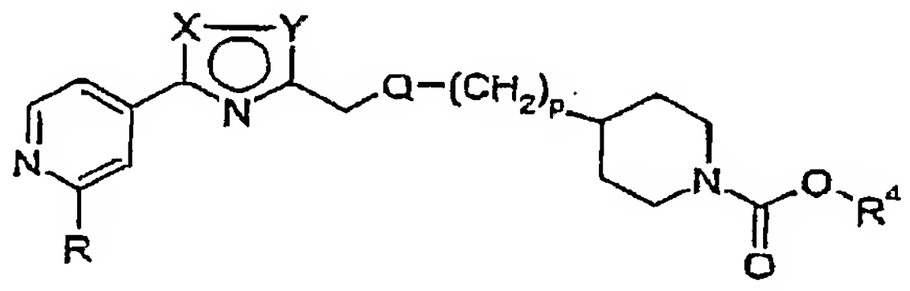
R^5 is hydrogen or C_{1-4} alkyl;

R^6 are independently hydrogen, or C_{1-4} alkyl, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^9, CN, SO_2CH_3, $N(R^{10})_2$ and NO_2; or a group $N(R^{10})_2$ may form a 4- to 7-membered heterocyclic ring optionally containing a further heteroatom selected from O and NR^{10};

R^9 is hydrogen, C_{1-2} alkyl or C_{1-2} fluoroalkyl; and

R^{10} is hydrogen or C_{1-4} alkyl.

10. A compound according to claim 1 having the formula (Ie), or a pharmaceutically acceptable salt thereof:



(Ie)

wherein one of X and Y is N, and the other is O;

Q is O, NR^5 or CH_2;

R is hydrogen, halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-7} cycloalkyl, aryl, OR^6, CN, NO_2, $S(O)_mR^6$, $CON(R^6)_2$, $N(R^6)_2$, $NR^{10}COR^6$, $NR^{10}SO_2R^6$, $SO_2N(R^6)_2$, a 4- to 7-membered heterocyclyl group or a 5- or 6-membered heteroaryl group;

R^4 is C_{2-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^5 is C_{1-4} alkyl;

R^6 are independently hydrogen, or C_{1-4} alkyl, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^9, CN, SO_2CH_3, $N(R^{10})_2$ and NO_2; or a group $N(R^{10})_2$

may form a 4- to 7-membered heterocyclic ring optionally containing a further heteroatom selected from O and NR^{10};

R^9 is hydrogen, C_{1-2} alkyl or C_{1-2} fluoroalkyl;

R^{10} is hydrogen or C_{1-4} alkyl; and

p is 0 or 1.

11. A pharmaceutical composition comprising a compound according to any one of claims 1 to 10, including the compound of proviso c), or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier.

12. A method for the treatment of a disease or condition in which GPR116 plays a role comprising a step of administering to a subject in need thereof an effective amount of a compound of the formula, or pharmaceutically acceptable salt thereof:

$$R^1\text{-}V\text{-}B\text{-}R^2$$

wherein V represents a 5-membered heteroaryl ring of the formula:

wherein W is N and one of X and Y is N and the other is O;

B is -CH=CH- or $(CH_2)_n$, where one of the CH_2 groups may be replaced by O, NR^5, $S(O)_m$, C(O) or $C(O)NR^{12}$;

n is 0, 1, 2 or 3;

m is independently 0, 1 or 2;

R^1 is 3- or 4-pyridyl, 4- or 5-pyrimidinyl or 2-pyrazinyl, any of which may be optionally substituted by one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-7} cycloalkyl, aryl, OR^6, CN, NO_2, $S(O)_mR^6$, $CON(R^6)_2$, $N(R^6)_2$, $NR^{10}COR^6$, $NR^{10}SO_2R^6$, $SO_2N(R^6)_2$, a 4- to 7-membered heterocyclyl group or a 5- or 6-membered heteroaryl group;

R^2 is 4- to 7-membered cycloalkyl substituted by R^3, $C(O)OR^3$, $C(O)R^3$ or $S(O)_2R^3$, or 4- to 7-membered heterocyclyl, containing one or two nitrogen atoms which is unsubstituted or substituted by $C(O)OR^4$, $C(O)R^3$, $S(O)_2R^3$, $C(O)NHR^4$, $P(O)(OR^{11})_2$ or a 5- or 6-membered nitrogen containing heteroaryl group;

R^3 is C_{3-8} alkyl, C_{3-8} alkenyl or C_{3-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be optionally substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^4 is C_{2-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be substituted with one or more

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substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^5 is hydrogen, $C(O)R^7$, $S(O)_2R^8$, C_{3-7} cycloalkyl or C_{1-4} alkyl optionally substituted by OR^6, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-2} alkyl, C_{1-2} fluoroalkyl, OR^6, CN, $N(R^6)_2$ and NO_2;

R^6 are independently hydrogen C_{1-4} alkyl, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^9, CN, SO_2CH_3, $N(R^{10})_2$ and NO_2; or a group $N(R^{10})_2$ may form a 4- to 7-membered heterocyclic ring optionally containing a further heteroatom selected from O and NR^{10};

R^7 is hydrogen, C_{1-4} alkyl, OR^6, $N(R^6)_2$, aryl or heteroaryl;

R^8 is C_{1-4} alkyl, C_{1-4} fluoroalkyl, aryl or heteroaryl;

R^9 is hydrogen, C_{1-2} alkyl or C_{1-2} fluoroalkyl;

R^{10} is hydrogen or C_{1-4} alkyl;

R^{11} is phenyl; and

R^{12} is hydrogen, C_{1-6} alkyl or C_{3-7} cycloalkyl.

13. A method for the treatment of a disease or condition in which GPR116 plays a role comprising a step of administering to a subject in need thereof an effective amount of a compound according to any one of claims 1 to 10, including the compounds of provisos a) to c), or a pharmaceutically acceptable salt thereof.

14. A method for the regulation of satiety comprising a step of administering to a subject in need thereof an effective amount of a compound according to any one of claims 1 to 10 or 12, including the compounds of provisos a) to c), or a pharmaceutically acceptable salt thereof.

15. A method for the treatment of obesity comprising a step of administering to a subject in need thereof an effective amount of a compound according to any one of claims 1 to 10 or 12, including the compounds of provisos a) to c), or a pharmaceutically acceptable salt thereof.

16. A method for the treatment of diabetes comprising a step of administering to a subject in need thereof an effective amount of a compound according to any one of claims 1 to 10 or 12, including the compounds of provisos a) to c), or a pharmaceutically acceptable salt thereof.